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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Hermann Oppermann

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ROPES & GRAY LLP
PATENT DOCKETING 39/361
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EXAMINER

LI, RUIXIANG

ART UNIT

PAPER NUMBER

1646

MAIL DATE

DELIVERY MODE

09/08/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/816,768	Applicant(s) OPPERMANN ET AL.	
	Examiner RUIXIANG LI	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 May 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) 1-5 and 10-19 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 6-8 is/are rejected.
- 7) ☒ Claim(s) 9 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

Applicant's amendment filed on 05/14/2009 has been entered. Claims 1-19 are pending. Claims 6-9 are currently under consideration. All other claims are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Withdrawn Objections and/or Rejections

The objection to the specification is withdrawn in view of Applicants' argument.

The rejections of claims 6-9, 20, and 21 under 35 U.S.C. 112, first paragraph for written description and scope of enablement are withdrawn in view of amended claims and canceled claims 20 and 21.

The rejection of claims 6-8 and 20 under 35 U.S.C. 102(b) as being anticipated by Hall et al. (WO 96/39430, 12 December 1996) is withdrawn in view of amended claims and canceled claim 20.

The rejection of claims 6-8 under 35 U.S.C. 102(e) as being anticipated by Nimni et al. (U.S. Patent No. 6,352,972 B1, March 5, 2002; 102(e): June 3, 1997) is made moot by canceled claims.

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The objection to claims 6-9 and 20 because they recite non-elected subject matter (TGF- β family proteins) is withdrawn in view of amended claims and canceled claim 20.

Claim Rejections under 35 U.S.C. §102

(i). The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(ii). Claims 6-8 are rejected under 35 U.S.C. 102(e) as being anticipated by Nimni et al. (U.S. Patent No. 6,352,972 B1, March 5, 2002; 102(e): June 3, 1997).

Nimni et al. teach a TGF- β fusion protein comprising a TGF- β 1 active fragment (the C-terminal domain of TGF- β 1) and a leader sequence. The leader sequence may comprise a purification tag, proteinase-sensitive linker sites and a protein binding domain such that the leader sequence may contain all or some of the following elements: purification tag:proteinase site: ECM binding site: proteinase site: TGF- β (page 4, the 2nd paragraph). Table 1 (column 5) lists various TGF- β 1 fusion proteins, such as a His-tagged C-terminal active fragment of TGF β 1 (Table I, lines 2; page 10, lines 3-4). Hall et al. teach that the refolded fusion protein under low concentrations o

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urea and DTT or a redox system used DTT in conjunction with glutathione had little or biological activity (Example 5, column 10, lines 44-57; column 11, lines 6-8). Hall et al. teach a fusion protein comprising the active portion of BMP proteins, such as OP-1, also called BMP-7 (column 2, line 22; column 3, lines 13-18). Since the fusion protein appears to satisfy the structural requirement, the additional properties recited in claims 6-8 are inherent to the structure of the fusion protein. Thus, the teachings of Nimni et al. meet the limitations of claims 6-8, 20, and 21.

(iii). Response to Applicants' argument

Applicants argue that claims have been amended to recite a latent OP-1 fusion protein. Applicants argue that Nimni et al. discloses specific TGF- β 1 and BMP-3 fusion proteins. Applicants argue that Nimni et al. disclose OP-1 (BMP-7) as one of the TGF- β 1 proteins that may be used, it does not disclose any specific examples of OP-1 fusion proteins. Applicants argue that Nimni et al. do not disclose that the renaturation of the TGF- β 1 fusion proteins under low concentrations of urea and DTT or a redox system using DTT in conjunction with glutathione resulted in properly refolded proteins. Applicants argue that Nimni et al. disclose that the TGF- β 1 fusion protein renatured using the modified glutathione redox system (method III) did have biological activity even when the leader sequence was present.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, the instant claims are not limited to specific OP-1 proteins;

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rather they are drawn to a genus of OP-1 fusion proteins. Since Nimni et al. teach a fusion protein comprising OP-1, the teaching of Nimni et al. meets the limitation.

Second, Nimni et al. teach that the activities of the refolded proteins depend upon the refolding conditions. For example, Hall et al. teach that the refolded fusion protein comprising a His-tagged C-terminal active fragment of TGF β 1 under low concentrations of urea and DTT or a redox system used DTT in conjunction with glutathione had little or biological activity (Example 5, page 13, lines 24-32; page 14, lines 18-20). However, refolded in the glutathione redox system involved a slow dilution of the urea-solubilized material with a balanced redox buffer (page 13, lines 8-12), the same fusion protein was biologically active (page 14, lines 18-20). Thus, whether a refolded TGF- β fusion is active or not depends not only upon the leader sequence, but also the refolding conditions and the formation of homodimers or heterodimers.

Moreover, since the fusion protein taught by Nimni et al. appears to satisfy the structural requirement, the additional properties recited in claims 6-8 are inherent to the structure of the fusion protein.

Conclusion

No claims are allowed.

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THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status

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information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/

Primary Examiner, Art Unit 1646

September 2, 2009